

**METHODS:** This retrospective cohort analysis utilized claims from a large national health plan. Included were members aged 65–89 years, with continuous enrollment between Jan-2008 and Dec-2009. Patients with T2DM (cases) were propensity matched 1:1 with non-diabetes patients (controls) by age, gender, ethnicity, geographic location, low-income status, and plan type. To assess burden of illness, all-cause health care costs for 2009 were calculated as the sum of all medical and pharmacy claims (based on ICD-9-CM and GPI codes), and were compared descriptively for cases and controls. In addition, costs directly attributable to diabetes were evaluated for the case cohort (based on ICD-9-CM 250.xx and prescriptions for anti-hyperglycemic agents). **RESULTS:** The analysis included 179,203 cases and matched controls. There were no significant differences at baseline between cohorts with respect to matched variables, however, cases had a significantly higher mean (SD) Deyo-Charlson Comorbidity Index compared to controls (2.47 versus 0.77 respectively;  $p < 0.0001$ ). Mean (SD) all-cause healthcare costs per patient per year were significantly higher for cases versus controls for in-patient hospitalization (\$1,120±\$4,425 vs. \$712±\$3,230), outpatient visits (\$5,475±\$15,640 vs. \$3,620±\$11,149), office visits (\$1,666±\$3,652 vs. \$1,358±\$3,492), ER visits (\$288±\$868 vs. \$219±\$759), pharmacy costs (\$2,195±\$2,807 vs. \$1,342±\$2,438) and total healthcare costs (\$10,406±\$19,959 vs. \$6,993±\$14,836) respectively, all  $p < 0.0001$ . The mean diabetes attributable total healthcare cost for the case cohort was \$3,588±\$9,270 per patient per year. **CONCLUSIONS:** All cause healthcare costs were significantly higher for patients with T2DM than for matched controls, highlighting the serious burden of illness in this Medicare Advantage population.

#### PDB65

##### ECONOMIC BURDEN OF CUSHING'S DISEASE: A POPULATION ANALYSIS OF DIRECT MEDICAL COSTS AND UTILIZATION

Swearingen B<sup>1</sup>, Wu N<sup>2</sup>, Chen SY<sup>2</sup>, Pulgar S<sup>3</sup>, Biller BMK<sup>1</sup>

<sup>1</sup>Massachusetts General Hospital, Boston, MA, USA, <sup>2</sup>United BioSource Corporation, Lexington, MA, USA, <sup>3</sup>Novartis Oncology, Florham Park, NJ, USA

**OBJECTIVES:** Cushing's disease (CD), a rare pituitary disorder, is associated with significant morbidity and mortality, but the economic impact is unknown. This study assessed the annual healthcare costs and utilization of CD patients. **METHODS:** Administrative claims from 2004–2008 of a large population with commercial or Medicare-supplemental insurance in the US were analyzed. CD patients were those with medical claims for Cushing's syndrome (ICD-9-CM: 255.0) and either benign pituitary adenoma (227.3) or hypophysectomy (07.6). Each CD patient was age- and gender-matched to four patients with non-functioning pituitary adenoma (NFPA) and ten population controls (PC). NFPA was identified as benign pituitary adenoma without Cushing's syndrome, acromegaly (253.0) or hyperprolactinemia (253.1). Comorbid conditions and annual direct healthcare costs were compared between cohorts by calendar year. **RESULTS:** The study identified 877 CD patients (79% female; average age 43 years). Hypertension (43% [CD] vs. 24% [NFPA] vs. 17% [PC]), diabetes (29% vs. 13% vs. 7%) and hyperlipidemia (27% vs. 21% vs. 14%) were the most common comorbidities in CD patients and more prevalent than in NFPA patients and PC (all  $p < 0.05$ ). CD patients had significantly higher total healthcare costs than NFPA patients and PC in 2004–2008; the difference between cohorts increased over time. In 2008, average healthcare costs were \$26,440 among CD patients, compared to \$13,708 in NFPA patients and \$5,954 in PC (both  $p < 0.05$ ). Approximately one-third of total costs among CD patients were attributable to CD-related services. CD patients were more likely to have inpatient admissions (20.7% vs. 15.8% [NFPA] vs. 7.1% [PC], both  $p < 0.01$ ), had more frequent outpatient hospital visits (6.5 vs. 3.8 vs. 1.8, both  $p < 0.01$ ), and received more medications than NFPA patients and PC (means: 10.0 vs. 7.4 vs. 4.7, both  $p < 0.01$ ). **CONCLUSIONS:** CD patients had more comorbidities than NFPA patients and PC, and incurred significantly higher annual healthcare costs.

#### PDB66

##### COSTS OF THE PHARMACEUTICAL PROGRAM TO TREAT T2DM PATIENTS FROM HIPERDIA: GOVERNMENT HEALTH CARE PROGRAM FOR DIABETES AND HYPERTENSION POPULATION UNDER THE BRAZILIAN PUBLIC HEALTH CARE SYSTEM

Nasciben V, Melo TG

Boehringer Ingelheim Brazil, Sao Paulo, Brazil

**OBJECTIVES:** Diabetes is a chronic disease that requires continuing care to reduce the risk of long-term complications. In this sense it is important to maintain a good therapeutic arsenal providing good treatment to maintain type 2 diabetes (T2DM) and hypertension under control, preventing complications. We decided to assess the costs of the HIPERDIA program with medication provided by the government for a future cost-effectiveness research. **METHODS:** HIPERDIA is a program for monitoring hypertensive and diabetic patients under care in the public healthcare system. Based on that database, we searched the number of patients under treatment from 2005 to 2010 and also the number of doses of the drugs (glibenclamide and metformin) available to control T2DM (Datusus/Hiperdia). Also, we looked at the Brazilian price database (Banco de Preços) the minimum and the maximum price paid by the government for those drugs to calculate their total costs in the program. **RESULTS:** From 2002 to 2010, we found a total of 1,067,754 patients using glibenclamide 5 mg and 662,519 patients under metformin 850 mg, however it was not clear the number of patients taking both. The average daily dose was 1.79 tablet for glibenclamide and 1.74 for metformin. In the price database from the government, we found that the average price paid for glibenclamide was R\$ 0.008/daily unit (ranging from R\$ 0.007 to 0.04) and for metformin R\$ 0.026/daily unit (ranging from R\$ 0.023 to 0.098). From January 2009 to August 2010 the total cost of this program with these 2 drugs reached R\$ 1,567,145 and our projections showed that, since 2002, the government spent about R\$ 9 million. **CONCLUSIONS:** Generics

generated a huge price pressure for those drugs in Brazil and with this scenario it seems to be difficult to predict the plans to update the drug list to provide more effective treatments for this population.

#### PDB67

##### IT PROCESSES IN CLINICAL PRACTICES FOR DIABETES PATIENTS TYPE II

Huttin C<sup>1</sup>, Atwood S<sup>2</sup>

<sup>1</sup>ENDEPUSresearch and ENDEPResearch Group, Cambridge, MA, USA, <sup>2</sup>Brigham and Women's Hospital, Boston, MA, USA

**OBJECTIVES:** This project presents an analysis of IT processes on variations of prescribing patterns for patients diagnosed with diabetes type II, following the first study on electronic billing and its association with diabetic drug prescribing (Huttin/Wong,2010). **METHODS:** A sample of 610 patients is extracted from the CDC physician survey. IT processes include electronic medical records (EMR), with or without patient demographics, computerized orders for Rx, tests, lab results, notes from nurses and physicians, public health reporting. Several hierarchical clustering methods are tested to identify various stages of IT processes and the impact of IT is analyzed with non parametric tests (analysis of variance) on prescribing patterns. **RESULTS:** Two HB clustering methods (average method and ward) identify three clusters representing different stages of IT processes: physicians using no IT at all (80.76%) and two levels of IT operations in practices (cluster 2: 17.33%; cluster 3: 1.91%). The dendrogram with the AL method presents clearer separation than the dendrogram with the ward method. Variations in drug prescribing is significant between clusters, using the scoring savage test: -21 for cluster 1, 16.85 for cluster 2, 4.4 for cluster 3 (P value 0.01). The analysis on new drugs does not show different prescribing patterns; however, the number of injectables (insulin) per patient is significantly higher in cluster 2 than 1 (0.51 versus 0.39). Different patterns of IT processes are also identified within cluster 2 and other clustering methods among grouping and similarity computations (e.g. Shusaku et al,2004) are tested to analyze the propagation of IT processes among the practices of this dataset (generalisation tested with a similarity matrix). **CONCLUSIONS:** This project can be used for analysis and management of IT processes inside clinical systems and control for their effects on physician prescribing behaviours. Results confirm that in addition to ebilling, different patterns of IT processes have an impact on treatment regimens (especially affecting insulin or insulin/OAD combinations). This can complement Koro et al study (2004).

#### PDB68

##### ASSESSING LIFEYEARS SAVED FROM 2000 TO 2010 IN CHINA DUE TO NOVO NORDISK INSULIN

Henriksen O, Jain P, Nielsen OK

Novo Nordisk, Inc., Bagsvaerd, Denmark

**OBJECTIVES:** Insulin and other diabetes treatments are generally considered cost effective treatment options as they reduce the incidence of complications, increase life expectancy and improve quality of life. This paper quantifies in a new model the life years saved in the Chinese diabetic population between 2000 and 2010 due to sales of Novo Nordisk insulin. **METHODS:** The CORE diabetes model was used to make projections of long-term survival rates for people with type 2 diabetes treated with defined therapies; modern insulin monotherapy (MI Mono), Modern Insulin combined with Oral Anti Diabetics (OAD), human insulin combined with OAD (HI OAD) and human insulin monotherapy (HI Mono). In the human insulin scenarios, the base case cohort characteristics were based on the Chinese DiabCare data for 1998 (mean age 56.71 years, 58% male, duration of diabetes 7 years, HbA1c 8.81%). The modern insulin scenarios (introduced around 2005) are based on cohort characteristics observed in the Chinese PRESENT study (mean age 57.21 years, 51% male, duration of diabetes 6 years, HbA1c 7.93%). Treatment effects in the four interventions modelled; MI Mono, MI OAD, HI OAD and HI Mono relied on published sources (HbA1c: -1%, -1.82%, -1.2% and 0.7% respectively). The annual size of the population treated was calculated using annual Novo Nordisk sales and average daily insulin dosage as observed in the DiabCare China study. This process was then repeated for each year from 2000 to 2010 making it possible to cumulate the number of life years saved. **RESULTS:** The undiscounted life expectancy for the 4 different baseline cohorts modelled in the CORE diabetes model was improved by 2.9, 2.7, 2.2, 1.7 for MI OAD, MI Mono, HI OAD, HI Mono respectively. **CONCLUSIONS:** The cumulated undiscounted life years saved between 2000 and 2010 was estimated at 136.198.66 due to treatment with Novo Nordisk insulin in China.

#### PDB69

##### EXENATIDE (BID) AND LIRAGLUTIDE (QD) TREATMENT PATTERNS AMONG TYPE-2 DIABETES PATIENTS IN GERMANY

Miller LA<sup>1</sup>, Burudpakdee C<sup>2</sup>, Zagar A<sup>1</sup>, Bhosle M<sup>3</sup>, Reaney M<sup>4</sup>, Schabert VF<sup>3</sup>

<sup>1</sup>Eli Lilly and Company, Indianapolis, IN, USA, <sup>2</sup>IMS Consulting, Falls Church, VA, USA, <sup>3</sup>IMS Health, Falls Church, VA, USA, <sup>4</sup>Eli Lilly and Company, Surrey, UK

**OBJECTIVES:** Exenatide and liraglutide are the two therapeutic options in the GLP-1 anti-diabetic medication class, to improve glycemic control in adults with type 2 diabetes (T2D). This study evaluated patient and prescriber characteristics, treatment patterns, average daily dose (ADD), and glycemic control of patients initiating GLP-1 medications in Germany. **METHODS:** The LifeLink™ EMR-EU database contains records for over 15 million German patients and 3,000 physicians. The cohort included patients who initiated exenatide or liraglutide during the index period (01/01/2009 - 04/30/2010). Patients also had ≥180 days history, pre-index; 90–540 days follow-up, post-index; and a T2D diagnosis (ICD-10 E10–E14), pre-index. Univariate tests were conducted at  $\alpha = .05$ . **RESULTS:** The cohort included 692 patients (exenatide 292, liraglutide 400): mean (SD) age 59 (±10) years, 59% male. Diabetologists prescribed liraglutide more frequently than exenatide (65% vs. 35%) compared to non-diabetologists (51% vs. 49%). Choice of GLP-1 was not associated with pa-

tient age, sex, number of pre-index antidiabetic medications ( $1.9 \pm 0.9$ ), pre-index HbA1c ( $8.2 \pm 1.5\%$ ), or Charlson Comorbidity Index ( $0.45 \pm 0.78$ , all  $p > .05$ ). Mean (SD) ADD was 16.7 mcg ( $\pm 9.22$ ; label range 10-20 mcg) for exenatide patients and 1.43 mg ( $\pm 0.69$ , label range 0.6-1.8 mg) for liraglutide patients. Among patients with post-index HbA1c tests, mean values did not differ at the first (7.9), second (7.8), or third (7.8, all  $p > .05$ ) tests. Exenatide patients were more likely than liraglutide patients to continue pre-index anti-diabetic medications (67.1% vs. 60.3%,  $p = .027$ ) or to start concomitant anti-diabetic medications at index (32.2% vs. 25.0%,  $p = .013$ ); however, exenatide patients were less likely to augment treatment post-index (15.8% vs. 22.5%,  $p = .027$ ). Post-index, 9.3% exenatide and 10% liraglutide patients discontinued GLP-1 therapy ( $p > .05$ ). **CONCLUSIONS:** Results suggest that some differences exist between German patients initiating exenatide or liraglutide, with respect to prescribing physician specialty, pre- and post-index treatment patterns, and ADD. Both GLP-1s show comparable post-index HbA1c.

#### PDB70

##### BASELINE CHARACTERISTICS AND ANTIDIABETIC EXPOSURE IN PATIENTS WITH TYPE-2 DIABETES TREATED WITH LIRAGLUTIDE

McAdam Marx C<sup>1</sup>, Bouchard J<sup>2</sup>, Aagren M<sup>3</sup>, Conner C<sup>3</sup>, Brixner D<sup>1</sup>

<sup>1</sup>University of Utah, Salt Lake City, UT, USA, <sup>2</sup>Novo Nordisk, Inc., Princeton, NJ, USA, <sup>3</sup>Novo Nordisk, Inc., Redmond, WA, USA

**OBJECTIVES:** This study describes baseline characteristics and prior antidiabetic therapy of patients in an electronic medical record (EMR) prescribed liraglutide, a once-daily GLP-1 agonist, relative to non-liraglutide patients. **METHODS:** Adults ( $\geq 18$  years) with T2DM, a new prescription for liraglutide from 3/10/2010 to 7/16/2010 (index date), and EMR activity  $\geq 395$  days pre-index to  $\geq 1$  day post-index were identified. Demographics, comorbidities, and pre-index antidiabetic prescriptions orders were compared to adults with T2DM,  $\geq 1$  non-liraglutide antidiabetic order from 1/1/2010 to 7/16/2010 (index date), and EMR activity  $\geq 395$  days pre-index to  $\geq 1$  day post-index. Bootstrapping was used to provide robust mean (95% CI) estimates for comparison patients due to sample size ( $n = 247,922$ ). **RESULTS:** Of 1,162 liraglutide patients, 58.8% were female and mean (95% CI) age was 55.5 (54.9, 56.2) years vs. 53.0% female and 60.9 (60.1, 61.6) years for comparison patients. For liraglutide vs. comparison patients, mean baseline HbA1c was 8.1% (8.0, 8.2) vs. 7.6% (7.5, 7.8), BMI was 38.3 kg/m<sup>2</sup> (37.8, 38.8) vs. 34.1 kg/m<sup>2</sup> (33.6, 34.6), body weight was 109.5 kg (108.0, 111.0) vs. 96.7 kg (95.1, 98.3). Comorbidities in liraglutide vs. comparison patients included dyslipidemia (87.1% vs. 79.2%), hypertension (73.6% vs. 73.8%), and cardiovascular disease (18.2% vs. 22.4%). Of liraglutide patients, 5.6% were antidiabetic drug naive pre-index vs. 42.0% of comparison patients. The most common antidiabetics prescribed any time the year pre-index were metformin and sulfonylureas, respectively, for liraglutide (64.5%, 37.5%) and comparison (28.7%, 19.6%) patients, followed by insulin (33.8% liraglutide vs. 19.6% comparison). Pre-index orders for multiple antidiabetics occurred in 75.6% of liraglutide and 22.5% of comparison patients ( $p \leq 0.01$  for all comparisons except hypertension  $p > .05$ ). **CONCLUSIONS:** Early data suggest that liraglutide is being utilized in very obese patients who failed to achieve HbA1c goal on other antidiabetics. Longitudinal research is warranted to assess liraglutide outcomes and changes in antidiabetics post-liraglutide.

#### PDB71

##### CHARACTERISTICS OF EARLY ADOPTERS OF EXPENSIVE MEDICATIONS

Juarez DT, Davis J, Fujimoto R, Chung RS

Hawaii Medical Service Association, Honolulu, HI, USA

**OBJECTIVES:** To examine characteristics of physicians who are early adopters of new expensive drugs **METHODS:** Retrospective analysis of pharmacy claims from 2006-2010 for 3 expensive diabetes drugs (exenatide, saxagliptin, and sitagliptin) identified by medical directors and pharmacists at large health plan in Hawaii. We examined how physician specialty and urban setting affected likelihood of being an early prescriber. We calculated total paid costs and days supply by quarter for each physician. We also examined whether same physicians tended to be early adopters of all drugs. **RESULTS:** Characteristics of early adopters differed by medication. For saxagliptin, during first 2 quarters, 53% of prescriptions were made by internists, 30% by general/family practitioners, 17% by other specialists and <1% by endocrinologists. This distribution stayed fairly stable over time. In contrast, for exenatide, in first 2 quarters usage was highest for endocrinologists (28%), Medicaid providers (29%) or other specialists (25%). By the end of 2010, however, most exenatide prescriptions were being made by internists or general/family practitioners. The trends for sitagliptin were similar to that of exenatide with endocrinologists (32%), Medicaid (34%) and other specialists (30%) being early adopters with a shift toward more prescriptions by primary care physicians. Early adopters tended to be in urban areas. 75% of physicians were early prescribers of one drug, 25% were early prescribers of two drugs, and none were early prescribers of all three medications. **CONCLUSIONS:** Research of this nature may enable us to target intervention programs to promote cost-effective prescribing patterns.

#### Diabetes/Endocrine Disorders – Research on Methods

#### PDB72

##### TWO-WAY INTERACTION EFFECT ANALYSIS OF DIABETES COMPLICATIONS ON HEALTH COSTS AND HEALTH OUTCOMES IN MEDICARE INPATIENTS

Wang X

University of Louisville, Louisville, KY, USA

**OBJECTIVES:** The purpose of this project is to investigate the interaction effects of diabetes complications on Medicare expenditures, length of hospitalization, claim frequency and mortality of diabetes inpatients in the Medicare population. **METHODS:** The analysis is based on inpatient claims data with 244,299 records for

the year 2004, from CMS (the Centers for Medicare and Medicare Services) chronic condition data warehouse. In this study, the RXMATCH function, summary statistics and 0-1 indicator functions are used to generate the predictor variables, heart disease, kidney disease, neurologic disorder, ocular disease and hypertension. The generalized linear model with a gamma distribution is employed for the analysis of interaction effects of complications on Medicare payments and length of stay (LOS). The Poisson regression model is applied to analyze the effects on the frequency of claims. The logistic regression model is utilized to study the effects on mortality. **RESULTS:** Results demonstrate that several two-way interactions such as heart disease and eye disease, heart disease and hypertension are significant to costs and LOS. The effects between kidney disease and cardiovascular disease are significant in the Poisson regression model. The interaction effect between renal disease and cardiovascular disease is significant to mortality. **CONCLUSIONS:** After the study, we can conclude that for inpatients with other diabetes complications, there are differences in health costs and health outcomes between the inpatients who have cardiovascular disease and those who do not have. There also exist big differences in outcomes between the patients who have renal disease and those who do not have.

#### PDB73

##### A CLAIMS-BASED EMPIRIC APPROACH TO ASSESSING MEDICATION POSSESSION FOR PATIENTS INITIATING THERAPY WITH INSULINS

Buysman E<sup>1</sup>, Conner C<sup>2</sup>, Liu F<sup>1</sup>, Aagren M<sup>3</sup>, Bouchard J<sup>4</sup>

<sup>1</sup>3 Innovus, Eden Prairie, MN, USA, <sup>2</sup>Novo Nordisk, Inc., Redmond, WA, USA, <sup>3</sup>Novo Nordisk, Inc., Princeton, NJ, USA, <sup>4</sup>Novo Nordisk, Inc., Plaisiow, NH, USA

**OBJECTIVES:** An important challenge addressing researchers studying adherence among insulin-requiring patients with diabetes is the discrepancy between the point-of-sale (POS) entered days supply and the actual time of medication possession. Significant deviation between these two can result in misleading medication possession ratio (MPR) estimates, especially in cases where the quantity dispensed is known to differ significantly, as is the case with insulin detemir delivered in a 15mL FlexPen® (IDetFP) pack versus NPH insulin delivered in a 10mL vial. This research expands upon an approach used by Klienman et al., and suggests an alternative measure of medication possession for insulins. **METHODS:** Data were gathered from a large US national payer retrospective claims database, and included only patients  $\geq 18$  years of age with type 2 diabetes that had  $\geq 2$  retail pharmacy fills of IDetFP or NPH vial in a 12-month observation period. Patients with claims for any other insulin, other than the index insulin during the 12-month observation period, were excluded. Median empirically-derived days supply (EDDS) estimates, based on median time-to-next-refill intervals, and POS entered days supplies were compared within and between cohorts. **RESULTS:** Median POS days supply estimates were identical for both the IDetFP and NPH cohorts, 30.00 days for both; however, median EDDS were significantly different between IDet and NPH cohorts, 45.00 vs. 36.00, respectively ( $p < 0.001$ ). In addition, within-group comparisons of POS days supply and EDDS in both cohorts revealed significant differences ( $p < 0.001$  for both tests). **CONCLUSIONS:** Drawing meaningful conclusions about adherence with insulins using pharmacy claims remains a significant challenge. Our analysis demonstrates that POS days supply entries, commonly used for adherence analysis, may deviate substantially and significantly from EDDS estimates. This study explores a novel, alternative, and empirically-based approach to determining medication possession. Research to further refine this and suggest other alternative methods should be encouraged.

#### PDB74

##### BETA-VERIFICATION OF A DIABETES MODELING FRAMEWORK AGAINST PUBLISHED COHORT TRIALS

Furiak N, Bansal M, Gahn JC, Smolen H

Medical Decision Modeling Inc., Indianapolis, IN, USA

**OBJECTIVES:** To perform a beta-verification of a novel diabetes modeling and analysis framework (DMAF) designed to accommodate growing demand for analysis on ever-shifting special subpopulations, new interventions, and updated care algorithms. A Monte Carlo microsimulation model assuming standard oral and subsequent insulin therapy generated mean outcomes as defined by recently published trials: 1) ACCORD-BPLI; 2) ACCORD-GLI; 3) ASPEN; and 4) ADVANCE. **METHODS:** Diabetes is increasing in prevalence, and its 20-year history of diabetes care has witnessed a shift from treating complications to prevention based on evidence from: The United Kingdom Prospective Diabetes Study, Diabetes Control and Complications Trials, and the Wisconsin Epidemiological Study of Diabetic Retinopathy. All have confirmed that tight control of hemoglobin A1c reduced the incidence of complications. Recent trials of diabetes have evaluated targeted interventions for clinical factors and impact on complication rates. Evidence from these trials suggests that aggressive A1c targets may not be suitable for all patients. The evolution of decision models for diabetes has paralleled that of care. Increased prevalence has placed pressure on health care costs and expectations that new interventions impart significant benefits. New evidence has in turn motivated development of decision models that evaluate new interventions, treatments, and care algorithms. **RESULTS:** The DMAF was reasonably consistent with well-defined composite endpoints for ASPEN (15.0% vs. 17.1%); ADVANCE: Secondary (10.5% vs. 9.6%), fatal MI (5.7% vs. 5.5%), all coronary events (11.9% vs. 10.3%); and ACCORD-BPLI non-fatal MI (1.4% vs. 1.3%). DMAF showed results within orders of magnitude for endpoints such as ASPEN angina (2.6% vs. 3.1%); ACCORD-BPLI: heart failure (0.5% vs. 0.8%), major coronary event (3.1% vs. 2.4%), primary outcome (3.6% vs. 2.1%); ACC ORD-GLI non-fatal MI (6.5% vs. 4.6%). **CONCLUSIONS:** Trial outcomes defined as "new or worsening" were not well-matched by DMAF due possibly to uncertainty in definitions and suitability for modeling.